REMARKS/ARGUMENTS

Claims 1-34 are pending in the captioned application. Claims 14-19 have been withdrawn. Applicants hereby cancel the non-elected kit claims 21-34. Claims 1-13 and 20 are therefore under examination and have been rejected. Applicants have cancelled claims 5, 8-9 and 20. Applicants respectfully request reconsideration and allowance of the claims in view of the amendments and the following arguments.

Claims 1-13 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Applicants respectfully disagree. However, in an effort to expedite prosecution, Applicants have amended the claims to clarify the invention, rendering the rejections moot.

The Examiner regards claim 1 as vague in steps iv) and v) because it was not clear how ligands can bind to intracellular analytes. In response, Applicants have amended claim 1 to include the limitation of claim 9 (i.e., the membranes of the cells are made permeable to ligands).

The Examiner also regards claim 1 step v) as confusing because, in the Examiner's view, "it is unclear how the binding agent comprising a specific binding pair is prevented from binding the ligands that have bound to cell-surface bound analyte or intracellularly bound analyte". In response, Applicants submit that at high linear flow rates cells or cell fragments does not readily migrate down to the sensor surface (see page 567, last paragraph, Fåhraeus and Lindqvist, Am. J. Physiol. 1931; 96:562-8), thus resulting in preferential binding of free ligands over cell (or cell

fragment) bound ligands. Thus ligands bound to cell-surface analytes or intracellular analytes will not bind to the sensor surface. Also when the ligands bind to intracellular analytes of a permeable cell the cell is not lysed and thus the cell is still intact when the ligand binds. Thus, only ligands which are not associated with cells or cell fragments may bind to the sensor surface.

The Examiner further regards step vi) of claim 1 as ambiguous and suggests that the amount of ligands used should be predetermined to allow a comparison. In response, Applicants have amended claim 1 to include the limitation of the now cancelled claim 5.

Claim 3 is rejected as lacking clear antecedent basis for the phrase "cell fragments". Claim 4 is similarly rejected. In response, claim 1 has been amended to recite that the cell sample-containing fluid contains intact cells and cell fragments. The rejection of these terms should therefore now be withdrawn.

Claim 3 is also rejected for the recitation that "cells and cell fragments are removed…". The Examiner questions whether Applicants intend to refer to those cells and cell fragments that have the antigens bound to ligands. Applicants have amended the claim to make clear that the cells and cell fragments include those that have ligands bound thereof.

Applicants submit that the 35 U.S.C. §112, second paragraph, rejection of the claims should now be withdrawn.

Claims 1-8 and 10-13 stand rejected under 35 U.S.C. §103 (a) as being unpatentable over Wahlstrom et al. (WO 96/38729) in view of Malmqvist et al.

(USPN 5,492,840). Claim 9 stand rejected under 35 U.S.C. §103(a) further in view of Williams et al. (USPN 6,495,333). Applicants respectfully disagree.

Applicants first submit that the claims have been amended. Claim 1 has been amended to include the limitations of claims 5, 8 and 9.

Applicants submit that other than the differences the Examiner identified, there are additional features that distinguish the presently claimed invention from that of the Wahlstrom et al. reference. Namely, the Wahlstrom et al. reference describes a competitive assay, the method of which relies upon a situation where antibody and pathogens are separated prior to analysis. This separation step is not required according to the claims of the invention. As discussed earlier, at high linear flow rates cells or cell fragments do not readily migrate down to the sensor surface. Therefore, they do not need to be separated from the cell sample fluid before the analysis (i.e., determination of binding of ligand to the solid support surface).

Applicants submit that Malmqvist et al. does nothing more to cure the deficiency of Wahlstrom et al. Further, although Malmqvist et al. describes bifunctional molecules, those molecules were designed for sensor surface preparation, not for the competition assay of the present invention. In the present claims, the combination of bifunctional reagents is used in an array format for identification of cell surface markers through competition, and there is no requirement for separation of free and bound bifunctional reagents before the analysis.

Thus, Applicants submit that the claims are not obvious in view of the combination of Wahlstrom et al. and Malmqvist et al.

Applicants respectfully assert that the claims are in allowable form and earnestly solicit the allowance of claims 1-4, 6-7 and 10-13.

Early and favorable consideration is respectfully requested.

Respectfully submitted,

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